

CLAIMS

1. A method for determining the presence or absence of a target nucleic acid sequence in a sample nucleic acid, the method comprising:

5 (a) exposing the sample to a detection agent comprising a metal surface associated with a SER(R)S active species (SAS) and with a target binding species (TBS),

(b) observing the sample/agent mixture using SER(R)S to detect any surface enhancement of the label,

10 characterised in that the binding of the TBS to the target sequence causes increased surface enhancement of the SAS.

2. A method as claimed in claim 1 wherein the metal surface is not itself capable of surface enhancement when present in the detection agent of step (a).

3. A method as claimed in claim 1 ~~or claim 2~~ wherein the detection agent is exposed to the sample in step (a) as two or more separate components.

4. A method as claimed in ^{claim 1} ~~any one of the preceding claims~~ wherein the detection agent comprises a first agent and a second agent each having a different TBS, each TBS being capable of binding to the target sequence, and wherein the binding of the first and second TBS to the target sequence brings a metal surface associated with each TBS into proximity thereby causing surface enhancement of an SAS associated with one or both of the metal surfaces.

5. A method as claimed in ^{claim 1} ~~any one of the preceding claims~~ wherein the detection agent comprises monodisperse

unaggregated colloidal metal particles associated with a TBS comprising a nucleic acid or nucleic acid analog which is complementary to all or part of the target sequence.

6. A method as claimed in claim 5 wherein the TBS comprises propargyl amino modified nucleic acid or peptide nucleic acid.

7. A method as claimed in claim 5 ~~or claim 6~~ wherein there are more than 1, 2, 3, 4, 5, 10, or 20 TBS per metal colloid particle.

8. A method as claimed in ^{claim 1} ~~any one of the preceding claims~~ wherein a surface seeking group (SSG) is used to promote chemi-sorption of the SAS and/or TBS to the metal surface.

9. A method as claimed in claim 8 wherein the SSG comprises the triazole group, more preferably the benzotriazole group.

10. A method as claimed in claim 8 ~~or claim 9~~ wherein the SSG is modified with a dye which is a SAS.

11. A method as claimed in claim 10 wherein the modified SSG is an azobenzotriazole.

12. A method as claimed in claim 10 ~~or claim 11~~ wherein the modified SSG is used to associate the TBS to the metal surface.

13. A method as claimed in claim 12 wherein the modified

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a SSG is conjugated to the TBS via a linker group.

14. A method as claimed in ^{claim 1} ~~any one of claims 1 to 11~~ wherein the SAS is present in greater than 2, 5, 10, 20,
5 30, 40, 50 or 100 fold excess over the TBS.

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a 15. A method as claimed in ^{claim 1} ~~any one of the preceding claims~~ wherein more than one target sequence is
10 determined using multiple detection agents having distinguishable SAS.

16. A method as claimed in claim 15 wherein the target
sequences share sequence identity, and wherein a common
first agent is used in conjunction with specific
15 distinguishable second agents which can discriminate between the remainder of the target sequences.

17. A method for detecting the presence of, or
selecting, or identifying, or phylogenetically
20 classifying, an organism, the method comprising use of a method as claimed in ^{claim 1} ~~any one of the preceding claims~~ wherein the target nucleic acid sequence is associated with that organism.

18. A method for diagnosing a disease, the method
comprising use of a method as claimed in ^{claim 1} ~~any one of the preceding claims~~ wherein the target nucleic acid sequence
25 is associated with that disease.

19. A method for isolating a nucleic acid encoding a
specific gene, the method comprising use of a method as
claimed in ^{claim 1} ~~any one of the preceding claims~~ wherein the
30 target sequence corresponds to a sequence associated

with, or within, that gene.

20. A process for producing a detection agent, the process comprising the step of combining unaggregated
5 metal particles with a SAS and a TBS, whereby said SAS and TBS associate with said metal particles via an SSG.

21. A detection agent comprising: an unaggregated metal particle, being associated with a SAS and with a TBS
10 via an SSG.

22. An agent as claimed in claim 21 comprising a first agent and a second agent each having a different TBS.

23. A composition comprising two or more detection agents as claimed in claim 21 ~~or claim 22~~, each having a distinctive SAS.

24. A system comprising the agent ^{of claim 21} ~~or composition of any one of claims 21 to 23~~ plus a nucleic acid sample.

25. An apparatus comprising a SERRS analyser plus an agent ^{of claim 21} ~~composition or system of any one of claims 21 to 24~~.

26. Use of the apparatus of claim 25 in the method of any one of claims ²¹ ~~1~~ to 19 comprising

27. A kit comprising the agent ^{at} ~~or composition of any one of claims 21 to 23~~ plus one additional material for practising the method of ^{claim 1} ~~any one of claims 1 to 19~~.

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